

## CLAIMS

1. A composition having improved palatability prepared by freeze drying a mixture comprising a) at least one pharmaceutically active substance having an unpleasant taste; and b) at least one non-lipidic taste masking association comprising: b1) at least one acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms and b2) at least one non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures, said masking associate being in a sufficient amount to improve the palatability of the active substance having an unpleasant taste, and c) at least one filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures, said composition comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on the dried mixture.
2. The composition of claim 1, wherein said acid is citric acid or fumaric acid.
3. The composition of claim 1 or 2, wherein said binder is selected from the group of pectin, gelatin, xanthan gum, and apple pectin, and their mixtures.
4. The composition of one of claims 1 to 3, wherein the filler is dextrose.
5. The composition of one of claims 1 to 4, wherein the pharmaceutically active substance is selected from the group consisting of

non steroidal anti-inflammatory drugs, antacids, analgesics, antalgics, sedatives, antipyretics, antispasmodics, coronary vasodilators, peripheral vasodilators, cerebral vasodilators, anti-injectives, antibiotics, antiparasitics, antineoplastics, anxiolytics, tranquilizers, CNS stimulating agents, antihistaminics, laxatives, drugs for digestive motricity, anticoagulant, drug for use in thyroid dysfunction, nutriments, nutritional adjuvants, immuno-depressives, cholesterol-lowering agents, hormones, sex hormones, enzymes, antianginal drugs, anti-migraine drugs, myorelaxants, hypoglycemics, anorexiant, expectorants, antitussives, decongestants, antinauseants, hematopoietic drugs, uricosurics, plant extracts, radio contrast media, anti-anginals, anti-anxiety drugs, anti-arrhythmics, anti-bacterials, anti-diarrhoeals, anti-depressants, anti-epileptics, anti-fungals, anti-hypertensives, anti-inflammatory agents, anti-virals, cardiac agents, contraceptives, cough suppressants, cytotoxics, decongestants, diuretics, drugs for genito-urinary disorders, drugs for asthma disorders, drugs for use in Parkinson's Disease, and related disorders, drugs for use in rheumatic disorders, hypnotics, minerals, vitamins, lipid lowering drugs and the like.

6. The composition of one of claims 1 to 5, wherein the pharmaceutically active substance is selected from the group consisting of piroxicam, piroxicam- $\beta$ -(cyclodextrine), ambroxol hydrochloride, paracetamol, domperidone, nimesulide, ibuprofen, morniflumate, apomorphine, and dihydroergocryptine.

7. The composition according to one of claims 1 to 6, wherein the pharmaceutically active substance is complexed with a cyclodextrin.

8. The composition according to one of claims 1 to 7, wherein the pharmaceutically active substance is piroxicam- $\beta$ -(cyclodextrine).

9. The composition of one of claims 1 to 6, wherein the pharmaceutically active substance is non-complexed piroxicam or paracetamol.

5           10. The composition according to one of claims 1 to 9, comprising between 5% and 10% by weight of the acid.

11. The composition according to one of claims 1 to 10, comprising between 6% and 16% by weight of the binder.

10

12. The composition according to one of claims 1 to 11, comprising between 20 and 80% by weight of the filler.

13. The composition according to one of claims 1 to 8 or 10 to 12,  
15 wherein the active substance is complexed piroxicam, and the weight ratio between the acid and binder is equal to or less than 1.

14. The composition according to one of claims 1 to 8 or 10 to 13,  
20 wherein the active substance is complexed piroxicam, and the acid is citric acid and the binder is apple pectin.

15. The composition according to one of claims 1 to 8 or 10 to 14,  
wherein the active substance is BCDP, and the percentage of acid, based  
on total weight, is between 5 and 10%, the percentage of the binder, based  
25 on total weight, is between 6 and 10% and the percentage of the filler,  
based on total weight, is between 20 and 30%.

16. The composition according to one of claims 1 to 8 or 10 to 15,  
wherein the active substance is BCDP, and the percentage of citric acid,  
30 based on total weight, is between 5 and 10%, the percentage of the pectin,

based on total weight, is between 6 and 10% and the percentage of the dextrose, based on total weight, is between 20 and 30%.

17. The composition according to one of claims 1 to 16, wherein  
5 the composition is a freeze-dried aqueous or hydroalcoholic gel.

18. The composition according to one of claims 1 to 17, wherein the composition is a free-flowing compressible powder.

10 19. The composition according to one of claims 1 to 18, wherein the composition is an oral pharmaceutical composition.

20. Sieved freeze dried particles comprising a) at least a pharmaceutically active substance which has an unacceptable taste; b) at  
15 least a non-lipidic taste masking association comprising: b1) at least an acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms and b2) at least a non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives,  
20 polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures; and c) at least a filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures,  
25 said particles comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on the dried mixture particles.

21. Free-flowing compressible powder-like freeze-dried particles  
30 comprising a) at least a pharmaceutically active substance which has an unacceptable taste; b) at least a non-lipidic taste masking association

comprising: b1) at least an acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms and b2) at least a non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullolan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures; and c) at least a filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures,

said particles comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on the dried mixture particles.

22. A process for the preparation of freeze-dried particles comprising a pharmaceutically active substance having an unpleasant taste, and a non-lipidic taste masking association comprising an acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms and a binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullolan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures, and a filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures, said process comprising the following steps:

- a) preparing an aqueous or hydroalcoholic solution or suspension of the active substance having an unpleasant taste;

- 5                   b)     preparing an aqueous or hydroalcoholic gel comprising said aqueous or hydroalcoholic solution or suspension and a non-lipidic binder, an acid, and a filler;
- c)     homogenizing the aqueous or hydroalcoholic gel obtained in step b);
- d)     freeze-drying said homogenized gel; and
- e)     recovering the freeze-dried material,
- 10     said particles comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on the dried mixture particles.

23. The process of claim 22, wherein the freeze-dried composition resulting from step d) is sieved and recovered.

15                   24. The process of claim 22 or 23, wherein the acid, the binder, and the filler provided in step b) are successively added, either simultaneously or extemporaneously, to the solution or suspension.

25                   25. The process of one of claims 22 to 24, wherein the at least one pharmaceutically active substance is BCDP.

20                   26. The process of one of claims 22 to 25, further comprising sieving the freeze-dried composition obtained from step d) through a mesh of between about 200  $\mu\text{m}$  to 5 mm.

25                   27. The process of one of claims 22 to 26, further comprising preparing a pharmaceutical oral composition comprising the recovered freeze-dried material from step e).

30                   28. A pharmaceutical composition having improved palatability, comprising:

a) at least one active substance having an unpleasant taste;

b1) at least an acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms; and

b2) at least one a non-lipidic binder selected from the group  
5 consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures; and

c) at least a filler selected from the group consisting of dextrose,  
10 lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures;

wherein said composition results from lyophilization of a homogeneous liquid or gel,

15 said freeze dried composition comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on said dried composition.

29. Pharmaceutical composition according to claims 28, comprising between 20 and 80% by weight of the filler.

20 30. Pharmaceutical composition according to claim 28 or 29, wherein the active substance is complexed piroxicam, and the weight ratio between the acid and binder is equal to or less than 1.

31. Pharmaceutical oral composition comprising freeze dried particles or material of claims 1 to 21 or obtained by the process of claims  
25 22 to 30.

32. The pharmaceutical composition of any of claims 28 to 31, in the form of a particulate material.

33. The pharmaceutical composition of any of claims 28 to 32, further comprising acceptable vehicle for a sachet form.

34. The pharmaceutical composition of any of claims 28 to 31, formed into a tablet.

- 5           35. A method for making a pharmaceutical material having improved palatability, comprising at least:
- preparing a homogeneous liquid or gel comprising
- a) at least one active substance having an unpleasant taste;
- b1) at least an acid selected from the group consisting of organic
- 10   acids containing 2 to 8 carbon atoms; and
- b2) at least one a non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained
- 15   sugars like xanthan, alginates, and their mixtures; and
- c) at least a filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures;
- 20           lyophilizing said liquid or gel,
- said composition resulting from the lyophilization of said homogeneous liquid or gel comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on said dried composition.
- 25           36. The composition according to claim 35, comprising between 20 and 80% by weight of the filler.
37. The composition according to claim 35 or 36, wherein the active substance is complexed piroxicam, and the weight ratio between the acid and binder is equal to or less than 1.



38. The method of any of claims 35 to 37 further comprising sieving and/or compressing the freeze-dried liquid or gel.

39. The method of any of claims 35 to 38, further comprising formulating an oral pharmaceutical composition from the lyophilized gel or  
5 liquid.

40. Method for making tablets comprising at least an active substance having an unpleasant taste comprising at least:

preparing a homogeneous liquid or gel comprising

b) at least one active substance having an unpleasant taste;

10 b1) at least an acid selected from the group consisting of organic acids containing 2 to 8 carbon atoms; and

b2) at least one a non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives,  
15 polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures; and

c) at least a filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their  
20 mixtures;

lyophilizing said liquid or gel,

said composition resulting from the lyophilization of said homogeneous liquid or gel comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler,  
25 based on said dried composition,

and compressing said composition resulting from the lyophilisation, with or without a sieving step.

41. Use of a non-lipidic taste masking association comprising: 1)  
30 at least one acid selected from the group consisting of organic acids

containing 2 to 8 carbon atoms and 2) at least one non-lipidic binder selected from the group consisting of pectin, gelatin, xanthan gum, guar gum, cellulose derivatives, soy derivatives, polysaccharides, pullulan, povidone and derivatives, polyethylene glycol, chitosan and its derivatives, fermentation obtained sugars like xanthan, alginates, and their mixtures, said masking associate being in a sufficient amount to improve the palatability of the active substance having an unpleasant taste, in the presence of at least one filler selected from the group consisting of dextrose, lactose, sucrose, fructose, galactose, starch, cellulose and its derivatives, polyols like mannitol, xylitol, sorbitol, maltodextrin, amino acids, and their mixtures, within a freeze dried mixture, said mixture comprising 5 to 16% by weight of said acid, 6 to 30% by weight of said binder and at least 20% by weight of said filler, based on said dried mixture, to improve the palatability of at least one pharmaceutically active substance having an unpleasant taste.